



# SEQUENCE LISTING

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<120> BLOOD-BRAIN BARRIER THERAPEUTICS

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<140> US 09/429,798  
<141> 1999-10-29

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<151> 1998-08-14

<160> 52

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<220>  
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<400> 1

Tyr Gly Gly Phe Met Lys  
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<223> Polymer connected to alpha-amino group

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<221> MOD\_RES  
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<223> Polymer connected to epsilon-amino group

<400> 2

Tyr Gly Gly Phe Met Lys  
1 5

<210> 3  
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<220>  
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<223> Polymer connected to alpha-amino group

<400> 3

Tyr Gly Gly Phe Met Lys  
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<210> 4  
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<220>  
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<223> AMIDATION

<400> 4

Phe Arg Trp Trp Tyr Lys  
1 5

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<220>  
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<223> AMIDATION

<400> 5

Arg Trp Ile Gly Trp Lys  
1 5

<210> 6  
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<223> AMIDATION

<220>  
<221> MISC\_FEATURE  
<222> (6)..(6)  
<223> Xaa can be any naturally occurring amino acid

<400> 6

Trp Trp Pro Lys His Xaa  
1 5

<210> 7  
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<220>  
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<220>  
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<223> AMIDATION

<220>  
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<222> (4)..(4)  
<223> Xaa is either Lys or Arg

<400> 7

Trp Trp Pro Xaa  
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<210> 8  
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<223> AMIDATION

<220>  
<221> MISC\_FEATURE  
<222> (6)..(6)  
<223> Xaa can be any naturally occurring amino acid

<400> 8

Tyr Pro Phe Gly Phe Xaa  
1 5

<210> 9  
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<220>  
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<220>  
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<222> (1)..(5)  
<223> Amino acids are in the D-form

<220>  
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<222> (6)..(6)  
 <223> n is 0 or 1  
  
 <220>  
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 <222> (7)..(7)  
 <223> Xaa is Gly or the D-form of any naturally occurring amino acid  
  
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 <223> Amidation  
  
 <400> 9

Ile Met Ser Trp Trp Gly Xaa  
 1 5

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<220>  
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 <222> (6)..(6)  
 <223> Xaa is Gly or the D-form of any naturally occurring amino acid

<220>  
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 <223> AMIDATION

<400> 10

Ile Met Thr Trp Gly Xaa  
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<210> 11  
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<220>  
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<220>  
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<222> (2)..(2)  
<223> Xaa is A1, wherein A1 is the D-form of Nve or Mle

<220>  
<221> MISC\_FEATURE  
<222> (3)..(3)  
<223> Xaa is B2, wherein B2 is Gly, Phe, or Trp

<220>  
<221> MISC\_FEATURE  
<222> (4)..(4)  
<223> Xaa is C3, wherein C3 is Trp or Nap

<220>  
<221> MOD\_RES  
<222> (4)..(4)  
<223> AMIDATION

<400> 11

Tyr Xaa Xaa Xaa  
1

B1  
<210> 12  
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<213> Artificial sequence

<220>  
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<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> Tyr has at its N-terminus a Me-x-H-y-N group, wherein x is 0, 1, or 2; and y is 0, 1, or 2, with the proviso that x and y is never greater than 2

<220>  
<221> MOD\_RES  
<222> (1)..(2)  
<223> The amine between the first Tyr and the second Tyr is methylated, wherein z is 0 or 1

<220>  
<221> MISC\_FEATURE  
<222> (3)..(3)  
<223> Xaa is Xaa-z, wherein Xaa is Phe, D-Phe or NHBzl, and wherein z is 0 or 1

<220>  
<221> MOD\_RES

<222> (3)..(3)  
<223> AMIDATION

<400> 12

Tyr Tyr Xaa  
1

<210> 13  
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<220>  
<223> Synthetic construct

<220>  
<221> MISC\_FEATURE  
<222> (4)..(4)  
<223> Xaa is D4, wherein D4 is Lys or Arg

<220>  
<221> MOD\_RES  
<222> (5)..(5)  
<223> His is His-z, wherein z is 0 or 1

B1  
<220>  
<221> MISC\_FEATURE  
<222> (6)..(6)  
<223> Xaa is Xaa-z, wherein Xaa is any naturally occurring amino acid  
and z is 0 or 1

<220>  
<221> MOD\_RES  
<222> (6)..(6)  
<223> AMIDATION

<400> 13

Trp Trp Pro Xaa His Xaa  
1 5

<210> 14  
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<222> (2)..(2)

<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 14

Tyr Xaa Phe Phe

1

<210> 15

<211> 4

<212> PRT

<213> Artificial sequence

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<222> (2)..(2)

<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>

<221> MOD\_RES

<222> (4)..(4)

<223> AMIDATION

<400> 15

Tyr Xaa Phe Phe

1

<210> 16

<211> 4

<212> PRT

<213> Artificial sequence

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<223> Synthetic construct

<220>

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<222> (1)..(1)

<223> Tyr is Tyr(N-alpha-Me), i.e. N-alpha-methyl tyrosine

<220>

<221> MISC\_FEATURE

<222> (2)..(2)

<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 16

Tyr Xaa Phe Phe

1



<210> 17  
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<220>  
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<222> (1)..(1)  
<223> Tyr is Tyr(N-alpha-Cmp), i.e. N-alpha-cyclopropylmethyltyrosine

<220>  
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<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 17

Tyr Xaa Phe Phe  
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<210> 18  
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<222> (1)..(1)  
<223> Tyr is Tyr(N-alpha-hex), i.e. N-alpha-hexyltyrosine

<220>  
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<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 18

Tyr Xaa Phe Phe  
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<210> 19  
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<223> Synthetic construct

<220>

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<222> (1)..(1)

<223> Tyr is Tyr(N-alpha-Et2), i.e. N-alpha-diethyltyrosine

<220>

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<222> (2)..(2)

<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 19

Tyr Xaa Phe Phe

1

<210> 20

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<212> PRT

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<222> (1)..(1)

<223> Tyr is Dmt, i.e. 2,6-dimethyltyrosine

<220>

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<222> (2)..(2)

<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 20

Tyr Xaa Phe Phe

1

<210> 21

<211> 4

<212> PRT

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<220>

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<222> (1)..(1)

<223> Tyr is Dmt, i.e. 2,6-dimethyltyrosine

<220>  
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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
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<400> 21

Tyr Xaa Phe Phe  
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<222> (1)..(1)  
<223> Tyr is H-Tyr(3-F), i.e. 3-fluorotyrosine

<220>  
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<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 22

Tyr Xaa Phe Phe  
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<223> Tyr is H-Tyr(3-Cl), i.e. 3-chlorotyrosine

<220>

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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid  
  
<400> 23

Tyr Xaa Phe Phe  
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<222> (1)..(1)  
<223> Tyr is H-Tyr (3-Br), i.e. 3-bromotyrosine

B |  
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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid  
  
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Tyr Xaa Phe Phe  
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<223> Tyr is Dmt, i.e. 2,6-dimethyltyrosine

<220>  
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<222> (2)..(2)  
<223> Xaa is Tic-psi-[CH2-], i.e.  
3-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

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<222> (2)..(3)  
<223> nonpetidyl bond

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<223> Tyr is Dmt, i.e. 2,6-dimethyltyrosine

<220>  
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<223> Xaa is Tic-psi-[CH2-], i.e.  
3-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
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<222> (2)..(3)  
<223> nonpeptidyl bond

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<222> (2)..(2)

<223> Xaa is Tic-psi-[CH2-], i.e.  
3-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>

<221> MOD\_RES

<222> (3)..(3)

<223> Phe is -NCH3]Phe, i.e. N-methylphenylalanine

<400> 27

Tyr Xaa Phe Phe

1

<210> 28

<211> 4

<212> PRT

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<220>

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<220>

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<222> (2)..(2)

<223> Xaa is Tic-psi-[CH2-], i.e.  
3-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>

<221> MOD\_RES

<222> (3)..(3)

<223> Phe is -NH]Hfe, i.e. homophenylalanine

<400> 28

Tyr Xaa Phe Phe

1

<210> 29

<211> 4

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic construct

<220>

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<222> (1)..(1)

<223> Tyr is Tyr(NMe), i.e. N-methyltyrosine

<220>

<221> MISC\_FEATURE

<222> (2)..(2)

<223> Xaa is Tic-psi-[CH2-], i.e.  
3-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>

<221> MOD\_RES

<222> (3)..(3)

<223> Phe is -NH]Hfe, i.e. homophenylalanine

<400> 29

Tyr Xaa Phe Phe

1

<210> 30

<211> 4

<212> PRT

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<223> Synthetic construct

<220>

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<222> (2)..(2)

<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>

<221> MOD\_RES

<222> (3)..(3)

<223> Gly is Phg, i.e. phenylglycine

<400> 30

Tyr Xaa Gly Phe

1

<210> 31

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<212> PRT

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<220>

<223> Synthetic construct

<220>

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<222> (2)..(2)

<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 31

Tyr Xaa Trp Phe

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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
<221> MOD\_RES  
<222> (4)..(4)  
<223> AMIDATION

<400> 32

Tyr Xaa Trp Phe  
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<220>  
<223> Synthetic construct

<220>  
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<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 33

Tyr Xaa His Phe  
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<210> 34  
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<223> Synthetic construct

<220>



<221> MISC\_FEATURE  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
<221> MOD\_RES  
<222> (3)..(3)  
<223> Ala is 2-Nal, i.e. 3-(2'-naphthyl)alanine

<400> 34

Tyr Xaa Ala Phe  
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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
<221> MISC\_FEATURE  
<222> (3)..(3)  
<223> Xaa is Atc, i.e. 2-aminotetralin-2-carboxylic acid

<400> 35

Tyr Xaa Xaa Phe  
1

<210> 36  
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<223> Synthetic construct

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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
<221> MOD\_RES  
<222> (4)..(4)

<223> Phe is Phe(pNO2), i.e. 4-nitrophenylalanine

<400> 36

Tyr Xaa Phe Phe  
1

<210> 37

<211> 4

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic construct

<220>

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<222> (2)..(2)

<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>

<221> MOD\_RES

<222> (4)..(4)

<223> Phe is Phe(pNO2), i.e. 4-nitrophenylalanine

<400> 37

Tyr Xaa Trp Phe  
1

<210> 38

<211> 4

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic construct

<220>

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<222> (2)..(2)

<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>

<221> MOD\_RES

<222> (4)..(4)

<223> AMIDATION

<400> 38

Tyr Xaa Phe Trp  
1

<210> 39  
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<212> PRT  
<213> Artificial sequence

<220>  
<223> Synthetic construct

<220>  
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<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
<221> MOD\_RES  
<222> (7)..(7)  
<223> AMIDATION

<400> 39

Tyr Xaa Phe Phe Val Val Gly  
1 5

<210> 40  
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<212> PRT  
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<220>  
<223> Synthetic construct

<220>  
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<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
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<222> (7)..(7)  
<223> AMIDATION

<400> 40

Tyr Xaa Phe Phe Tyr Pro Ser  
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<210> 41  
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<213> Artificial sequence

<220>

<223> Synthetic construct

<220>

<221> MISC\_FEATURE

<222> (2)..(2)

<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>

<221> MOD\_RES

<222> (7)..(7)

<223> AMIDATION

<400> 41

Tyr Xaa Trp Phe Tyr Pro Ser

1

5

<210> 42

<211> 7

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic construct

<220>

<221> MISC\_FEATURE

<222> (2)..(2)

<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>

<221> MOD\_RES

<222> (4)..(4)

<223> Phe is Phe(pNO2), i.e. 4-nitrophenylalanine

<220>

<221> MOD\_RES

<222> (7)..(7)

<223> AMIDATION

<400> 42

Tyr Xaa Trp Phe Tyr Pro Ser

1

5

<210> 43

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<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic construct

<220>  
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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
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<222> (6)..(6)  
<223> Nle

<220>  
<221> MOD\_RES  
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<223> AMIDATION

<400> 43

Tyr Xaa Phe Phe Leu Leu Asp  
1 5

<210> 44  
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<212> PRT  
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<223> Synthetic construct

<220>  
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<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 44

Tyr Xaa Phe  
1

<210> 45  
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<220>  
<223> Synthetic construct

<220>  
<221> MISC\_FEATURE  
<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>

<221> MOD\_RES  
<222> (3)..(3)  
<223> AMIDATION

<400> 45

Tyr Xaa Phe

1

<210> 46  
<211> 3  
<212> PRT  
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<220>  
<223> Synthetic construct

<220>  
<221> MISC\_FEATURE  
<222> (2)..(2)  
<223> Xaa is Tic-psi-[CH2-], i.e.  
3-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
<221> MOD\_RES  
<222> (2)..(3)  
<223> nonpeptidyl bond

<400> 46

Tyr Xaa Phe

1

<210> 47  
<211> 4  
<212> PRT  
<213> Artificial sequence

<220>  
<223> Synthetic construct

<220>  
<221> MISC\_FEATURE  
<222> (2)..(2)  
<223> Xaa is Tic-psi-[CH2-], i.e.  
3-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>  
<221> MOD\_RES  
<222> (2)..(3)  
<223> nonpeptidyl bond

<400> 47

Tyr Xaa Phe Phe  
1

<210> 48  
<211> 5  
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<213> Artificial sequence

<220>  
<223> Synthetic construct

<400> 48

Tyr Gly Gly Phe Met  
1 5

<210> 49  
<211> 6  
<212> PRT  
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<220>  
<223> Synthetic construct

<400> 49

Tyr Gly Gly Phe Met Lys  
1 5

<210> 50  
<211> 6  
<212> PRT  
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<220>  
<223> Synthetic construct

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> NH2 of Tyr is blocked by butyloxycarbonyl group

<400> 50

Tyr Gly Gly Phe Leu Lys  
1 5

<210> 51  
<211> 6  
<212> PRT  
<213> Artificial sequence

<220>  
<223> Synthetic construct

<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> NH2 of Tyr is blocked by butyloxycarbonyl group

<400> 51

Tyr Gly Gly Phe Leu Lys  
1 5

<210> 52  
<211> 6  
<212> PRT  
<213> Artificial sequence

<220>  
<223> Synthetic construct

*B1*  
*anal*  
<220>  
<221> MOD\_RES  
<222> (1)..(1)  
<223> NH2 of Tyr is blocked by butyloxycarbonyl group

<220>  
<221> MOD\_RES  
<222> (6)..(6)  
<223> Polymer connected to epsilon-amino group

<400> 52

Tyr Gly Gly Phe Leu Lys  
1 5